

REMARKS

The Amendment, filed in response the Office Action mailed September 11, 2009, is believed to fully address all and every issue raised in the Office Action. Reconsideration on the merits and allowance of the application are respectfully requested.

Claims Disposition and Summary of Amendments

Claims 10-17 and 19-22 are all the claims pending in the application.

In the instant Amendment, independent claims 14-17 are amended to further define the chiral catalyst. Support for the amended claims may be found by the disclosure of Examples 4 and 9 ($\text{Ru}_2\text{Cl}_4[(\text{S})\text{-H}_8\text{-binap}]_2\text{NEt}_3$) and Example 11 ($[\text{RuCl}(\text{p-cymene})((\text{S})\text{-dm-segphos})]\text{Cl}$). No new matter is introduced. Entry and consideration of amendments are respectfully requested.

Withdrawn Rejections

The Examiner has withdrawn rejections under 35 U.S.C. § 112, first paragraph, in view of Applicants' amendments and arguments. Applicants extend their appreciation.

Response to Claim Rejection Under 35 U.S.C. § 103

It is noted that the Office asserts that the previous rejection of claims 10-17 and 19-22 under 35 U.S.C. § 103 over US '037, in view of JACS '98 was proper. Page 4, lines 13-15.

Nevertheless, in the Office Action of September 11, 2009, the Office modifies the rejection of claims 10-17 and 19-22 by citing new references.

Applicants respectfully disagree with the previous rejections and instant rejections.

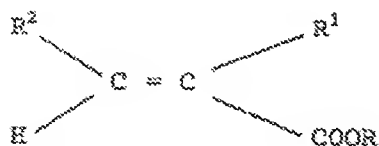
Nevertheless, solely in order to compact the prosecution, Applicants have amended independent claims 14-17 by further defining the types of a chiral catalyst.

1. Summary of Rejection

In the currently outstanding Office Action, claims 10-17 and 19-22 are rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Andersson et. al., US 6,258,850 patent, in view of Nohira, EP 408338 patent.

Andersson is cited as teaching successful asymmetric hydrogenation on several compounds, with chiral rhodium complexes and other metal catalysts. The Office admits that Andersson does not teach chiral ruthenium complexes as a chiral catalyst.

Nohira is cited as teaching that rhodium and ruthenium chiral complexes are effectively used for asymmetric hydrogenation of different compounds, such as α,β -unsaturated carboxylic acids (Abstract; p. 3, lines 23-47; p. 5, lines 10-13). The Office asserts that Nohira teaches that ruthenium and rhodium complexes with the 2,2'-bis(dicyclohexylphosphino)-6,6'-dimethyl-1,1'-biphenyl (BICHEP) ligand are effective catalysts for the asymmetric hydrogenation of α,β -unsaturated carboxylic acids, such as those compounds of formula (II) below (p. 3, lines 23-47; p. 3, line 48-p. 4, line 24; p. 5, lines 10-13):



where R^2 =phenyl group, etc.; R^1 =lower alkyl group; $\text{R}=\text{H}$, etc. The Office further asserts that Nohira teaches that Rh or Ru (BICHEP) chiral complexes catalyze asymmetric hydrogenation reactions to give products of high optical purity and yield (p. 14, lines 1-8).

Based on the above, the Office asserts that it would have been prima facie obvious for one of ordinary skill in the art, at the time of the invention, to carry out the asymmetric hydrogenation process of compounds taught by Andersson with Ru(BICHEP) chiral catalysts, because Andersson teaches that compounds such as those instantly claimed can successfully undergo asymmetric hydrogenation with chiral catalysts such as Rh-BINAP, [Et-DuPHOSRh(COD)], and Nohira teaches that Rh and Ru chiral complexes are both effective for asymmetric hydrogenation reactions. In particular, the Office assert that different types of catalysts (e.g., chiral Ru(BICHEP), Rh-BINAP, [Et-DuPHOSRh(COD)]) are taught as being effective for asymmetric hydrogenation, it would have been obvious to use these catalysts for asymmetric hydrogenation reactions on the substrates taught by Andersson due to their equivalence in performing this reaction.

2. Applicants' Responses

Claims 14-17 are amended to more clearly define the types of the chiral catalyst.

On the merits, Applicants submit the following arguments.

The claimed subject matter and the teaching of cited reference should be considered as a whole. Also, the teachings of cited reference should be considered in view of other contrary evidence offered by Applicants. In this regard, Applicants respectfully submit that the teachings of Andersson is contrary from what known in the art and understood by one skilled in the art.

As pointed out by the Office, Andersson states "The asymmetric reduction can be carried out using a wide variety of reducing methods known to reduce carbon-carbon double bonds such as catalytic hydrogenation in the presence of an appropriate chiral catalyst such as Rh-BINAP [Et-DuPHOS-Rh(COD)] or " (column 8, lines 17-24). However, the knowledge available at or around the time when the invention was made provide a different guidance.

For example, Angew. Chem. Int. Ed. 2007, 46, 4141-4144 describes "The Rh-catalyzed enantioselective hydrogenation of 3-aryl-2-ethoxyacrylic acids is usually extremely difficult" (page 4142, the 13th line from the bottom of right column).

In addition, according to Adv. Synth. Catal. 2006, 348, 1271-1276, asymmetric hydrogenation of α -methylcinnamic acid derivatives catalyzed by (R)-**1e** results in more than 90% ee (see Scheme 3 on page 1273), although asymmetric hydrogenation of (Z)- α -methoxycinnamic acid with catalyst (R)-**1e** results in 71% ee.

Furthermore, Org. Lett., Vol. 7, No.10, 2005, 1947-1950 describes "Despite the explosion in the development of chiral ligands for the asymmetric hydrogenation of a variety of olefin derivatives, relatively few examples exist for the successful reduction of α -alkoxy cinnamoyl derivatives" (page 1948, the 8th line from the bottom of right column) and "Similarly to the Duphos family of ligands, Jopishos and BiNAP derivatives (13 and 15-18 in Figure 1)

gave either low conversion or low enantiomeric excess under our conditions. Gratifyingly, the Rh-based systems using the aforementioned ligand motifs afforded conversions and asymmetric induction between 70 and 80% ee" (page 1949, lines 12-17). The above three references are listed in concurrently submitted IDS and copies are included.

Therefore, even after the filing date of the present application, contrary to the general statement of Andersson, on which the Office relies on to deny patentability of the claimed subject matter, it has been recognized that asymmetric hydrogenation of α -alkoxycinnamic acid is more difficult than asymmetric hydrogenation of α -alkylcinnamic acid. Indeed, Andersson does not show any working example of direct asymmetric reduction of α -alkoxycinnamic acid. Andersson discloses the following process: i) an ester of α -alkoxycinnamic acid is nonstereoselectively hydrogenated (Pd/C is used as a catalyst in Example 1(d) and rhodium on charcoal is used as a catalyst in Example 2(b)); ii) the resulting racemic body is hydrolyzed (Example 1(e) and Example 2(c)); and iii) the desired stereoisomer is separated by crystallization (Example 1(f)) or using silica gel column (Example 2(d)).

Accordingly, Applicants respectfully submit that one skilled in the art, who have general knowledge of the related art available in the art when or around when the invention was made, would not have been motivated to modify the teachings of Andersson, either alone or in combination with Nohira, to reach the claimed subject matter, with reasonable expectation of success, because such was not predicted.

In addition, Applicants respectfully submit that, according to the disclosure of the instant application, Example 4 and Example 11, both use the chiral catalyst recited in the amended

claims, accomplish about 90% ee and 88.6% , respectively. That is, the present invention results in a high optical purity.

In conclusion, the claimed subject matter is patentable over Andersson in view of Nohira, and withdrawal of the rejection is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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